

CLAIMS

What is claimed is:

1. A compound represented by the structural formula:



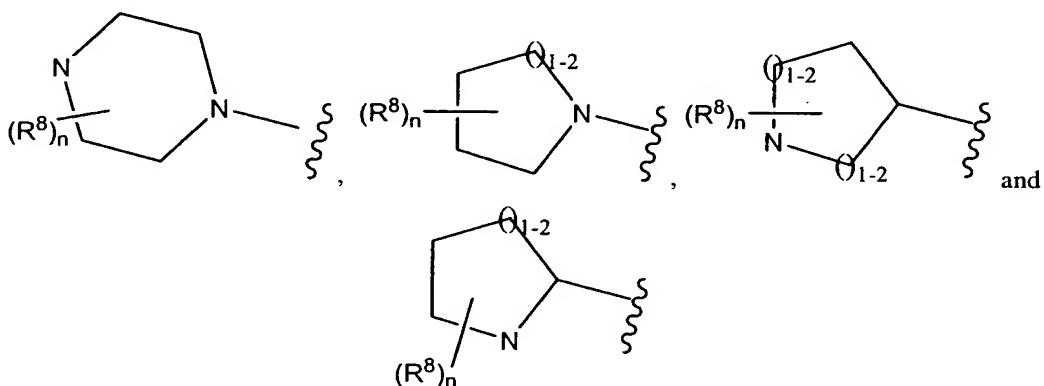
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Formula III

wherein:

R is selected from the group consisting of H, halogen, aryl, heteroaryl, cycloalkyl, arylalkyl, heterocyclyl, heterocyclalkyl, alkenyl, alkynyl, -C(O)R<sup>7</sup>,

10



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wherein each of said aryl, heteroaryl, cycloalkyl, arylalkyl, alkenyl, heterocyclyl and the heterocyclyl moieties whose structures are shown immediately above for R can be unsubstituted or optionally independently substituted with one or more

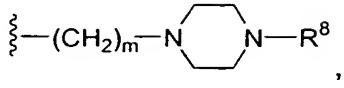
moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, cycloalkyl, CF<sub>3</sub>, CN, -OCF<sub>3</sub>, -OR<sup>6</sup>, -C(O)R<sup>7</sup>, -NR<sup>5</sup>R<sup>6</sup>, -C(O<sub>2</sub>)R<sup>6</sup>, -C(O)NR<sup>5</sup>R<sup>6</sup>, -(CHR<sup>5</sup>)<sub>n</sub>OR<sup>6</sup>, -SR<sup>6</sup>, -S(O<sub>2</sub>)R<sup>7</sup>, -S(O<sub>2</sub>)NR<sup>5</sup>R<sup>6</sup>, -N(R<sup>5</sup>)S(O<sub>2</sub>)R<sup>7</sup>, -N(R<sup>5</sup>)C(O)R<sup>7</sup> and -N(R<sup>5</sup>)C(O)NR<sup>5</sup>R<sup>6</sup>;

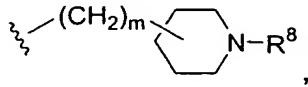
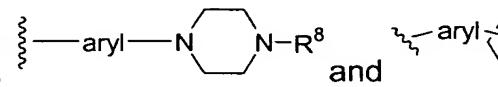
R<sup>1</sup> is H, halogen or alkyl;

20

R<sup>2</sup> is selected from the group consisting of halogen, R<sup>9</sup>, alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl, alkenyl, alkynyl, cycloalkyl,

$-\text{CF}_3$ ,  $-\text{C}(\text{O})\text{R}^7$ , alkyl substituted with 1-6  $\text{R}^9$  groups which groups can be the same

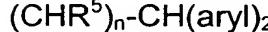
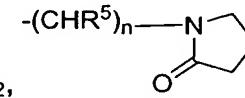
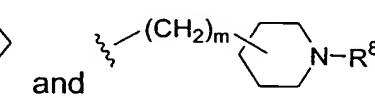
or different with each  $\text{R}^9$  being independently selected, 

  and  , wherein each of

said aryl, heteroaryl, arylalkyl and heterocyclyl can be unsubstituted or optionally

5 independently substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, cycloalkyl,  $\text{CF}_3$ ,  $\text{CN}$ ,  $-\text{OCF}_3$ ,  $-\text{OR}^6$ ,  $-\text{C}(\text{O})\text{R}^7$ ,  $-\text{NR}^5\text{R}^6$ ,  $-\text{C}(\text{O}_2)\text{R}^6$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^6$ ,  $-\text{SR}^6$ ,  $-\text{S}(\text{O}_2)\text{R}^7$ ,  $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^6$ ,  $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ ,  $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$  and  $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^6$ ;

10  $\text{R}^3$  is selected from the group consisting of  $\text{H}$ , aryl, heteroaryl, heterocyclyl,  $-(\text{CHR}^5)_n\text{-aryl}$ ,  $-(\text{CHR}^5)_n\text{-heteroaryl}$ ,  $-(\text{CHR}^5)_n\text{-OR}^6$ ,  $-\text{S}(\text{O}_2)\text{R}^6$ ,  $-\text{C}(\text{O})\text{R}^6$ ,  $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^6$ ,  $-\text{C}(\text{O})\text{OR}^6$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^6$ , cycloalkyl,  $-\text{CH}(\text{aryl})_2$ ,  $-(\text{CH}_2)_m\text{-NR}^8$ ,  $-(\text{CHR}^5)_n\text{-N}$

  and  , wherein each of

said aryl, heteroaryl and heterocyclyl can be substituted or optionally substituted

15 with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl,  $\text{CF}_3$ ,  $\text{CN}$ ,  $-\text{OCF}_3$ ,  $-\text{OR}^5$ ,  $-\text{NR}^5\text{R}^6$ ,  $-\text{C}(\text{O}_2)\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^6$ ,  $-\text{SR}^6$ ,  $-\text{S}(\text{O}_2)\text{R}^6$ ,  $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^6$ ,  $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ ,  $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$  and  $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^6$ ;

20  $\text{R}^5$  is  $\text{H}$  or alkyl;

$\text{R}^6$  is selected from the group consisting of  $\text{H}$ , alkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl, wherein each of said alkyl, heteroarylalkyl, aryl, heteroaryl and arylalkyl can be unsubstituted or optionally substituted with one or more moieties which can be the same or different, each moiety being

25 independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl,  $\text{CF}_3$ ,  $\text{OCF}_3$ ,  $\text{CN}$ ,  $-\text{OR}^5$ ,  $-\text{NR}^5\text{R}^6$ ,  $-\text{CH}_2\text{OR}^5$ ,  $-\text{C}(\text{O}_2)\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^6$ ,  $-\text{SR}^6$ ,  $-\text{S}(\text{O}_2)\text{R}^7$ ,  $-\text{S}(\text{O}_2)\text{NR}^5\text{R}^6$ ,  $-\text{N}(\text{R}^5)\text{S}(\text{O}_2)\text{R}^7$ ,  $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{R}^7$  and  $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{NR}^5\text{R}^6$ ;

$R^7$  is selected from the group consisting of alkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl, wherein each of said alkyl, heteroarylalkyl, aryl, heteroaryl and arylalkyl can be unsubstituted or optionally substituted with one or more moieties which can be the same or different, each moiety being independently

5 selected from the group consisting of halogen, alkyl, aryl, cycloalkyl,  $CF_3$ ,  $OCF_3$ ,  $CN$ ,  $-OR^5$ ,  $-NR^5R^6$ ,  $-CH_2OR^5$ ,  $-C(O_2)R^5$ ,  $-C(O)NR^5R^6$ ,  $-SR^6$ ,  $-S(O_2)R^7$ ,  $-S(O_2)NR^5R^6$ ,  $-N(R^5)S(O_2)R^7$ ,  $-N(R^5)C(O)R^7$  and  $-N(R^5)C(O)NR^5R^6$ ;

$R^8$  is selected from the group consisting of  $R^6$ ,  $-C(O)NR^5R^6$ ,  $-S(O_2)NR^5R^6$ ,  $-C(O)R^7$ ,  $-C(O_2)R^6$ ,  $-S(O_2)R^7$  and  $-(CH_2)\text{-aryl}$ ;

10  $R^9$  is selected from the group consisting of halogen,  $CN$ ,  $NR^5R^6$ ,  $-C(O_2)R^6$ ,  $-C(O)NR^5R^6$ ,  $-OR^6$ ,  $-C(O)R^7$ ,  $-SR^6$ ,  $-S(O_2)R^7$ ,  $-S(O_2)NR^5R^6$ ,  $-N(R^5)S(O_2)R^7$ ,  $-N(R^5)C(O)R^7$  and  $-N(R^5)C(O)NR^5R^6$ ;

$m$  is 0 to 4;

$n$  is 1-4; and

15  $p$  is 0-3.

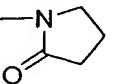
2. The compound of claim 1, wherein  $R$  is selected from the group consisting of H, halogen, aryl, heteroaryl, alkenyl and  $-C(O)R^7$ , wherein each of said aryl and heteroaryl can be unsubstituted or optionally independently substituted with one or more moieties which can be the same or different, each moiety being

20 independently selected from the group consisting of halogen, alkyl,  $CF_3$ ,  $CN$ ,  $-OCF_3$ , and  $-OR^6$ ;

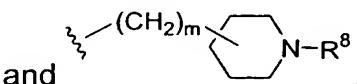
$R^1$  is H or lower alkyl;

$R^2$  is selected from the group consisting of halogen, alkyl, aryl, heteroaryl, alkenyl and  $-C(O)R^7$ , wherein each of said alkyl, aryl and heteroaryl can be unsubstituted or optionally independently substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl,  $CF_3$ ,  $CN$ ,  $-OCF_3$ , and  $-OR^6$ ;

$R^3$  is selected from the group consisting of H, aryl, heteroaryl,  $-(CHR^5)_n$ -aryl,  $-(CHR^5)_n$ -heteroaryl,  $-(CHR^5)_n$ - $OR^6$ ,  $-C(O)R^6$ , cycloalkyl,  $-CH(aryl)_2$ ,

$-(CHR^5)_n$ -

and



$N-R^8$ , wherein each of said aryl and

heteroaryl can be substituted or optionally substituted with one or more moieties

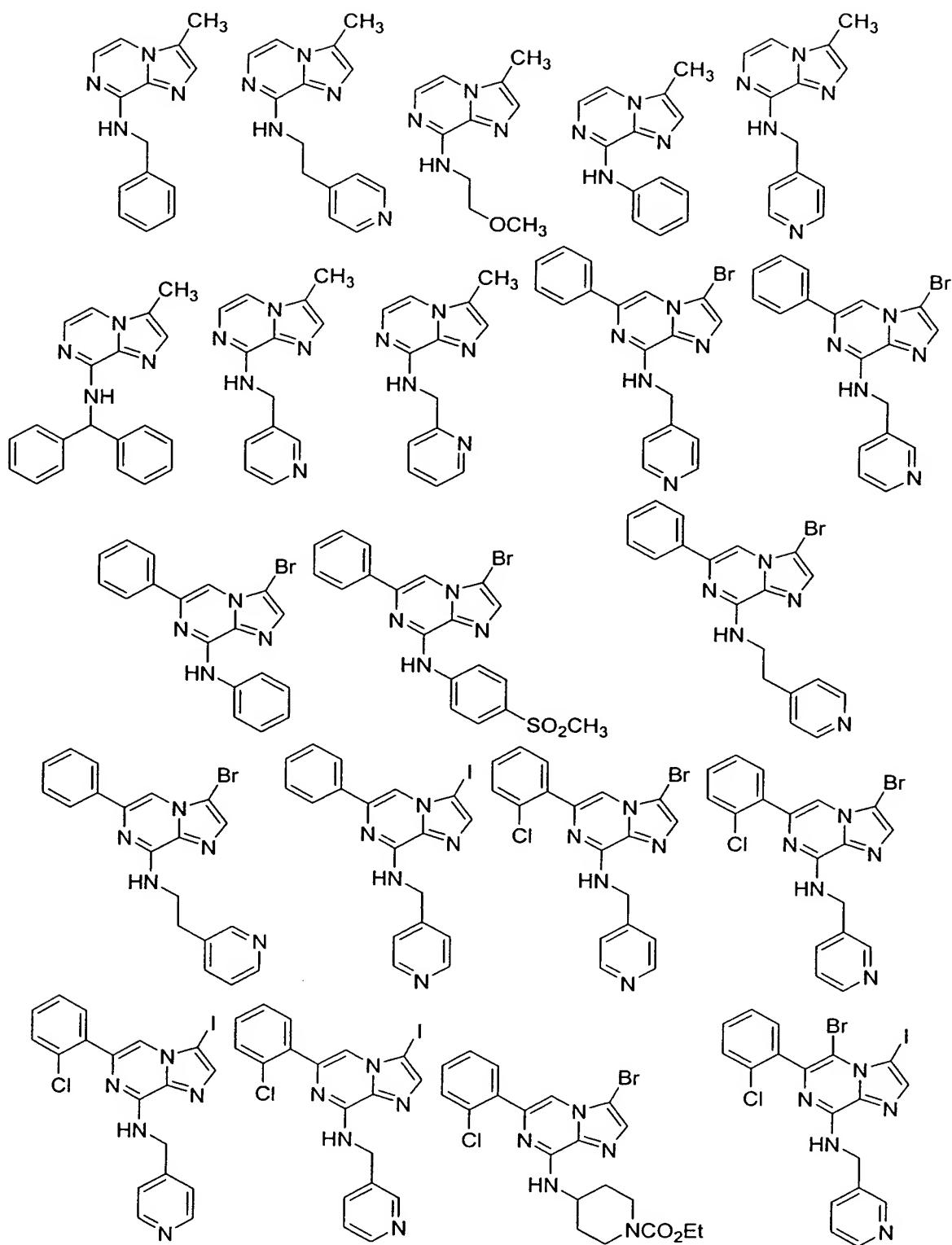
which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, aryl,  $CF_3$ ,  $CN$ ,  $-C(O_2)R^5$  and  $-S(O_2)R^6$ ;

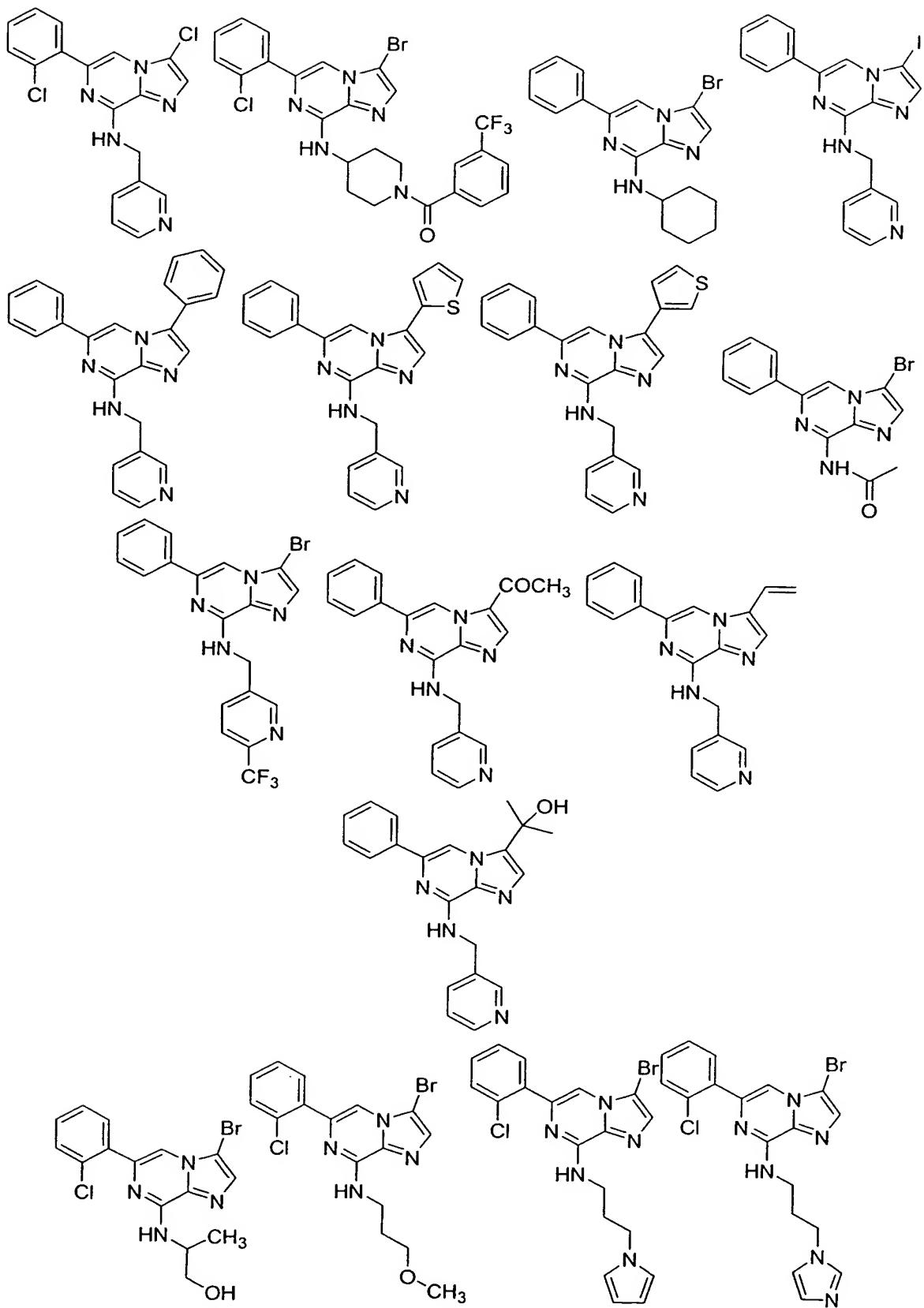
$R^5$  is H or lower alkyl;

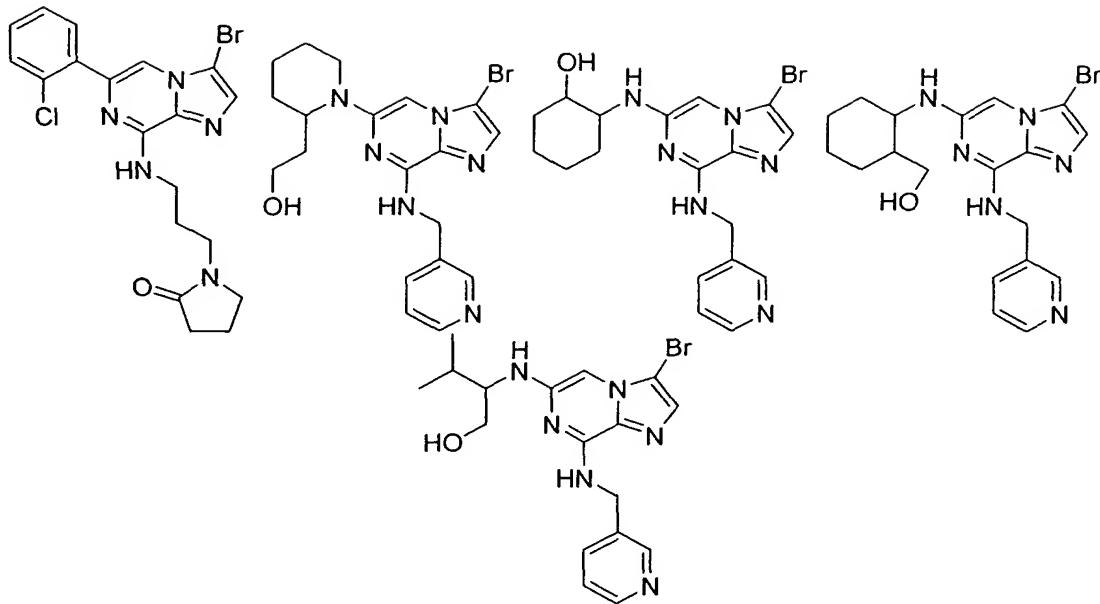
$m$  is 0 to 2; and

5       $n$  is 1 or 2.

3.      The compound of claim 2, wherein R is H.
4.      The compound of claim 2, wherein R is unsubstituted phenyl.
5.      The compound of claim 2, wherein R is phenyl substituted with one or more moieties selected from the group consisting of F, Cl, Br and  $OCF_3$ .
- 10     6.      The compound of claim 2, wherein  $R^2$  is F, Cl, Br, I, methyl, ethenyl, or  $-C(CH_3)_2-OH$ .
7.      The compound of claim 6, wherein  $R^2$  is Br, I or methyl.
8.      The compound of claim 2, wherein  $R^3$  is H, 2-ylpropanol, phenyl, benzyl, (pyrid-2-yl)methyl, (pyrid-3-yl)methyl, (pyrid-4-yl)methyl, 2-[(pyrid-3-yl)]ethyl and 2-15     [(pyrid-4-yl)]ethyl wherein each of said phenyl (including phenyl of said benzyl) and pyridyl can be unsubstituted or optionally independently substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of F, Cl, Br,  $CF_3$ , lower alkyl,  $-S(O_2)CH_3$ , methoxy and  $CN$ .
- 20     9.      The compound of claim 8, wherein  $R^3$  is benzyl.
10.     The compound of claim 8, wherein  $R^3$  is (pyrid-2-yl)methyl.
11.     The compound of claim 8, wherein  $R^3$  is (pyrid-3-yl)methyl.
12.     The compound of claim 8, wherein  $R^3$  is (pyrid-4-yl)methyl.
13.     The compound of claim 8, wherein  $R^3$  is 2-ylpropanol.
- 25     14.     The compound of claim 8, wherein  $R^3$  is 3-yl-propyl-1-pyrrolidin-2-one,
15.     The compound of claim 2, wherein  $R^3$  is phenyl.
16.     The compound of claim 2, wherein  $m$  is 0.
17.     A compound of the formula:

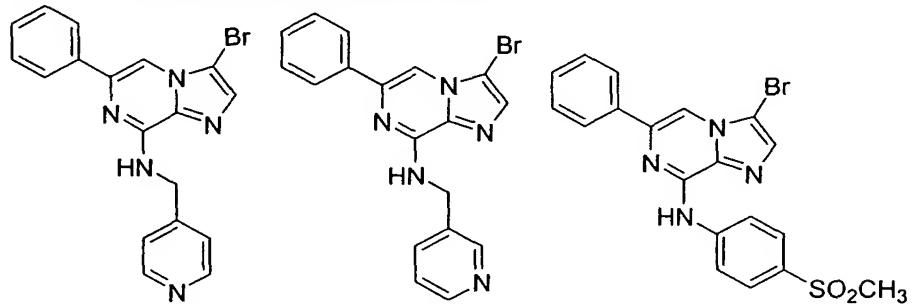


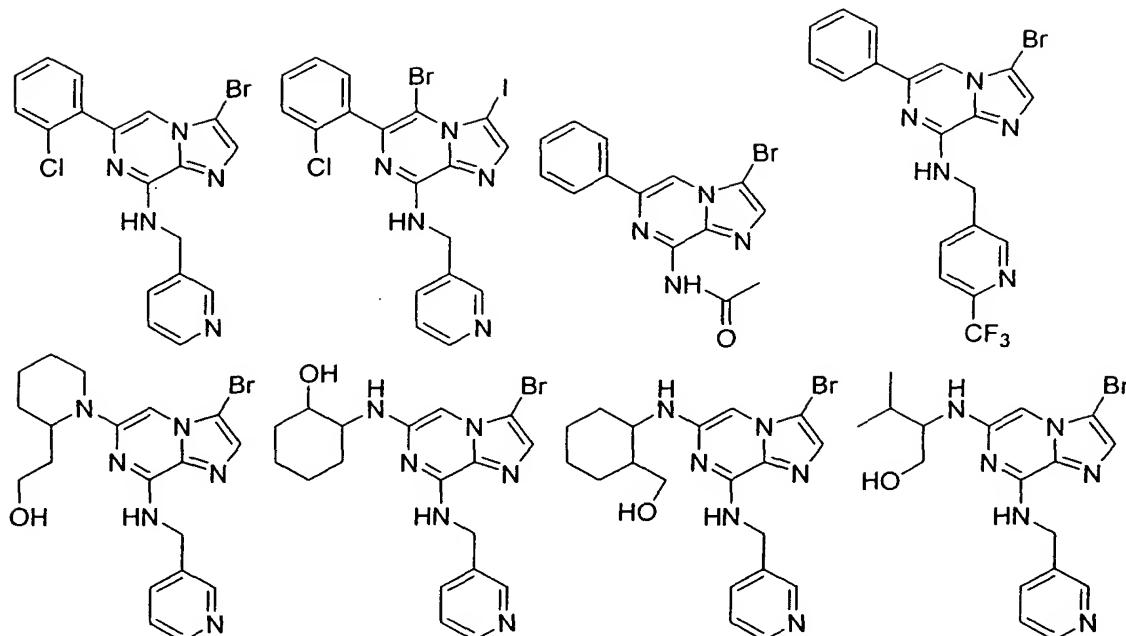




5 or a pharmaceutically acceptable salt or solvate thereof.

18. A compound of the formula:





or a pharmaceutically acceptable salt or solvate thereof.

5 19. A method of inhibiting one or more cyclin dependent kinases, comprising administering a therapeutically effective amount of at least one compound of claim 1 to a patient in need of such inhibition.

20. A method of treating one or more diseases associated with cyclin dependent kinase, comprising administering a therapeutically effective amount of at least one compound of claim 1 to a patient in need of such treatment.

10 21. The method of claim 20, wherein said cyclin dependent kinase is CDK2.

22. The method of claim 20, wherein said cyclin dependent kinase is mitogen activated protein kinase (MAPK/ERK).

15 23. The method of claim 20, wherein said cyclin dependent kinase is glycogen synthase kinase 3 (GSK3beta).

24. The method of claim 20, wherein said disease is selected from the group consisting of:

cancer of the bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid,

20 prostate, and skin, including squamous cell carcinoma;

leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T- cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphoma;

acute and chronic myelogenous leukemia, myelodysplastic syndrome and  
5 promyelocytic leukemia;

fibrosarcoma, rhabdomyosarcoma;

astrocytoma, neuroblastoma, glioma and schwannomas;

melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma  
pigmentosum, keratoctanthoma, thyroid follicular cancer and Kaposi's sarcoma.

10 25. A method of treating one or more diseases associated with cyclin  
dependent kinase, comprising administering to a mammal in need of such  
treatment

an amount of a first compound, which is a compound of claim 1, or a  
pharmaceutically acceptable salt or solvate thereof;

15 and

an amount of at least one second compound, said second compound being  
an anti-cancer agent;

wherein the amounts of the first compound and said second compound  
result in a therapeutic effect.

20 26. The method of claim 25, further comprising radiation therapy.

25 27. The method of claim 25, wherein said anti-cancer agent is selected from  
the group consisting of a cytostatic agent, cisplatin, doxorubicin, taxotere, taxol,  
etoposide, CPT-11, irinotecan, camptostar, topotecan, paclitaxel, docetaxel,  
epothilones, tamoxifen, 5-fluorouracil, methotrexate, 5FU, temozolomide,  
cyclophosphamide, SCH 66336, R115777, L778,123, BMS 214662, Iressa,  
Tarceva, antibodies to EGFR, Gleevec, intron, ara-C, adriamycin, cytoxan,  
gemcitabine, Uracil mustard, Chlormethine, Ifosfamide, Melphalan, Chlorambucil,  
Pipobroman, Triethylenemelamine, Triethylenethiophosphoramine, Busulfan,  
Carmustine, Lomustine, Streptozocin, Dacarbazine, Floxuridine, Cytarabine,  
30 6-Mercaptopurine, 6-Thioguanine, Fludarabine phosphate, oxaliplatin, leucovirin,  
ELOXATIN™, Pentostatine, Vinblastine, Vincristine, Vindesine, Bleomycin,  
Dactinomycin, Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Mithramycin,

Deoxycyformycin, Mitomycin-C, L-Asparaginase, Teniposide 17 $\alpha$ -Ethinylestradiol, Diethylstilbestrol, Testosterone, Prednisone, Fluoxymesterone, Dromostanolone propionate, Testolactone, Megestrolacetate, Methylprednisolone, Methyltestosterone, Prednisolone, Triamcinolone, Chlorotrianisene,

5 Hydroxyprogesterone, Aminoglutethimide, Estramustine, Medroxyprogesteroneacetate, Leuprolide, Flutamide, Toremifene, goserelin, Cisplatin, Carboplatin, Hydroxyurea, Amsacrine, Procarbazine, Mitotane, Mitoxantrone, Levamisole, Navelbene, CPT-11, Anastrazole, Letrazole, Capecitabine, Reloxafine, Droxofine, or Hexamethylmelamine.

10 28. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 1 in combination with at least one pharmaceutically acceptable carrier.

29. The pharmaceutical composition of claim 28, additionally comprising one or more anti-cancer agents selected from the group consisting of a cytostatic agent,

15 cisplatin, doxorubicin, taxotere, taxol, etoposide, CPT-11, irinotecan, camptostar, topotecan, paclitaxel, docetaxel, epothilones, tamoxifen, 5-fluorouracil, methotrexate, 5FU, temozolomide, cyclophosphamide, SCH 66336, R115777, L778,123, BMS 214662, Iressa, Tarceva, antibodies to EGFR, Gleevec, intron, ara-C, adriamycin, cytoxan, gemcitabine, Uracil mustard, Chlormethine,

20 Ifosfamide, Melphalan, Chlorambucil, Pipobroman, Triethylenemelamine, Triethylenethiophosphoramine, Busulfan, Carmustine, Lomustine, Streptozocin, Dacarbazine, Flouxuridine, Cytarabine, 6-Mercaptopurine, 6-Thioguanine, Fludarabine phosphate, Pentostatine, Vinblastine, Vincristine, Vindesine, Bleomycin, Dactinomycin, Daunorubicin, Doxorubicin, Epirubicin, Idarubicin,

25 Mithramycin, Deoxycyformycin, Mitomycin-C, L-Asparaginase, Teniposide 17 $\alpha$ -Ethinylestradiol, Diethylstilbestrol, Testosterone, Prednisone, Fluoxymesterone, Dromostanolone propionate, Testolactone, Megestrolacetate, Methylprednisolone, Methyltestosterone, Prednisolone, Triamcinolone, Chlorotrianisene, Hydroxyprogesterone, Aminoglutethimide, Estramustine,

30 Medroxyprogesteroneacetate, Leuprolide, Flutamide, Toremifene, goserelin, Cisplatin, Carboplatin, Hydroxyurea, Amsacrine, Procarbazine, Mitotane,

Mitoxantrone, Levamisole, Navelbene, CPT-11, Anastrazole, Letrazole, Capecitabine, Reloxafine, Droloxafine, or Hexamethylmelamine.

30. A compound of claim 1 in purified form.